

IN THE CLAIMS:

Amend the claims as follows.

1. (Withdrawn) Protein vaccine which comprises a mixture of viral protein molecules, **characterized in that** the molecules are sequence variants of a single viral protein or of part of same, the mixture containing $\geq 10^2$ sequence variants, which is obtainable by expression of a plasmid-DNA mixture which, because of the variation of nucleotide positions, contains randomly distributed sequence combinations.

2. (Withdrawn) Protein vaccine according to claim 1, **characterized in that** the mixture contains $\geq 10^3$ and preferably $\geq 10^4$ sequence variants.

3. (Withdrawn) Protein vaccine according to claim 1, characterized in that it comprises a mixture of GP120 proteins of HIV which in each case differ from each other in their amino acid sequence in the region of the V2 loop and/or of the V3 loop.

4. (Currently Amended) DNA vaccine which codes for a mixture of structurally different virus proteins, **characterized in that** the vaccine contains a mixture of sequence variants of a viral DNA molecule or of part of same, the mixture containing $\geq 10^2$ DNA molecules which differ from each other in their nucleic acid sequence, where the mixture, because of the variation of nucleotide positions, contains randomly distributed sequence combinations which result in different translation products upon expression.

5. (Original) DNA vaccine according to claim 4, **characterized in that** it contains a mixture of DNA molecules which code for the sequence variants of a viral protein or a part.

6. (Previously Presented) DNA vaccine according to claim 4, characterized in that the mixture contains $\geq 10^3$ and preferably $\geq 10^4$ DNA molecules which differ from each other in their nucleic acid sequence.

7. (Previously Presented) DNA vaccine according to claim 4, characterized in that it codes for a mixture of structurally different GP120 proteins of HIV, in which the vaccine contains a mixture of DNA molecules, the nucleic acid sequences of which differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop.

8. (Original) DNA vaccine according to claim 7, **characterized in that** it contains a mixture of DNA molecules which differ from each other in their nucleic acid sequence such that they code for a mixture of GP120 proteins which contain amino acid sequences which differ from each other in the V2 loop and/or in the V3 loop.

9. (Withdrawn) Nucleic acid sequence which is derived from the *env* sequence represented in SEQ ID NO: 1 or a fragment of same, **characterized in that** it is modified such that it contains monovalent restriction sites which make possible the specific exchange of the V2 and V3 regions.

10. (Withdrawn) Nucleic acid sequence which is derived from the *env* sequence represented in SEQ ID NO: 1 or a fragment of same, **characterized in that** it is modified such that it contains ten monovalent restriction cleavage sites at intervals of approx. 150 base pairs.

11. (Withdrawn) Nucleic acid sequence according to claim 9 , characterized in that the sequence is modified by the introduction of silent mutations.

12. (Withdrawn) Nucleic acid sequence according to claim 9, characterized in that it contains the sequence given in SEQ ID NO: 9.

13. (Withdrawn) Nucleic acid sequence, **characterized in that** it contains the sequence given in SEQ ID NO: 11.

14. (Withdrawn) Nucleic acid sequence, **characterized in that** it contains the sequence given in SEQ ID NO: 12.

15. (Withdrawn) Single-stranded nucleic acid sequence which contains the region coding for the V3 loop and/or for the V2 loop of GP120, **characterized in that** in the V3 loop a 247 bp-long BglII-XbaI fragment or a 283 bp-long BglII-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-Bc1I fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment,

the fragment/the fragments in each case containing inosine, a nucleic acid exchange or a mutation at at least 6 positions.

16. (Withdrawn) Single-stranded nucleic acid sequence which contains the region coding for the V2 loop and/or the region of GP120 coding for the V3 loop, **characterized in that** in the V3 loop a 247 bp-long Bg1II-XbaI fragment or a 283 bp-long Bg1II-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-Bc1I fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing inosine, a nucleic acid exchange or a mutation at at least 6 positions, the nucleic acid sequence being complementary to the nucleic acid sequence according to claim 14.

17. (Withdrawn) Nucleic acid sequence according to claim 15 or a single-stranded nucleic acid sequence which contains the region coding for the V2 loop and/or the region of GP120 coding for the V3 loop, characterized in that in the V3 loop a 247 bp-long Bg1II-XbaI fragment or a 283 bp-long Bg1II-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-Bc1I fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing inosine, a nucleic acid exchange or a mutation at at least 6 positions, the nucleic acid sequence being complementary to a nucleic acid sequence characterized in that it contains the sequence given in SEQ ID NO: 12 , characterized in that the fragment/the fragments contain(s) inosine, a nucleic acid exchange or a mutation at 9 to 20 positions.

18. (Withdrawn) Double-stranded DNA which comprises hybrids of the single-stranded nucleic acid sequence according to claim 15 with a single-stranded nucleic acid sequence which contains the region coding for the V2 loop and/or the region of GP120 coding for the V3 loop, characterized in that in the V3 loop a 247 bp-long Bg1II-XbaI fragment or a 283 bp-long Bg1II-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-BclI fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing inosine, a nucleic acid exchange or a mutation at at least 6 positions, the nucleic acid sequence being complementary to a nucleic acid sequence characterized in that it contains the sequence given in SEQ ID NO: 12.

19. (Withdrawn) Nucleic acid mixture which comprises double-stranded DNAs, the nucleic acid sequences of which are derived from the *env* sequence in SEQ ID NO: 1 or SEQ ID NO: 11 or a fragment of same, **characterized in that** the nucleic acid sequences in each case differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop.

20. (Withdrawn) Nucleic acid mixture according to claim 19, **characterized in that** the nucleic acid sequences differ from each other such that they code for a mixture of proteins which in each case contain amino acid sequences which differ from each other in the V2 loop and/or in the V3 loop.

21. (Withdrawn) Nucleic acid mixture according to claim 20, **characterized in that** the mixture contains $\geq 10^2$ sequence variants.

22. (Withdrawn) Nucleic acid sequence according to claim 21, **characterized in that** the mixture contains $\geq 10^3$ and preferably $\geq 10^4$ sequence variants.

23. (Withdrawn) Protein mixture which comprises sequence variants of the GP120 protein, **characterized in that** it is a mixture of proteins which contain amino acid sequences which in each case differ from each other in the V2 loop and/or in the V3 loop, the mixture being obtainable by expression of a plasmid DNA mixture which, because of the variation of nucleotide positions, contains randomly distributed sequence combinations.

24. (Withdrawn) Protein mixture according to claim 23, **characterized in that** the mixture contains $\geq 10^2$ sequence variants.

25. (Withdrawn) Protein mixture according to claim 24, **characterized in that** the mixture contains $\geq 10^3$ and preferably $\geq 10^4$ sequence variants.

26. (Withdrawn) Plasmid, which contains an inserted double-stranded DNA according to claim 18.

27. (Withdrawn) Expression vector, characterized in that it contains an inserted nucleic acid sequence according to claim 9.

28. (Withdrawn) Expression vector according to claim 27, **characterized in that** it contains the sequence given in SEQ ID NO: 10.

29. (Withdrawn) Expression vector, **characterized in that** it corresponds to DSM 12612.

30. (Withdrawn) Vector mixture which contains a mixture of plasmids according to claim 26, **characterized in that** the nucleic acid sequences of the plasmids differ in each case from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop, where the mixture of the plasmids, because of the variation of nucleotide positions, contains randomly distributed sequence combinations.

31. (Withdrawn) Vector mixture according to claim 30, **characterized in that** the mixture contains $\geq 10^2$ plasmids which differ from each other in their nucleic acid sequence.

32. (Withdrawn) Vector mixture according to claim 31, **characterized in that** the mixture contains $\geq 10^3$ and preferably $\geq 10^4$ plasmids which differ from each other in their nucleic acid sequence.

33. (Withdrawn) Vector mixture according to claim 30, characterized in that the plasmids can be expressed in *E. coli* as host cell.

34. (Withdrawn) Vector mixture according to claim 30, characterized in that the plasmids can be expressed in eukaryotic cells, preferably in Cos, CHO or BHK cells, as host cells.

35. (Withdrawn) *E. coli* host cells which are transfected with a vector mixture according to claim 33.

36. (Withdrawn) Eukaryotic host cells which are transfected with a vector mixture according to claim 34.

37. (Withdrawn) Eukaryotic host cell according to claim 36, **characterized in that** they are a host cell from the group consisting of Cos, BHK or CHO cells.

38. (Withdrawn) Process for the preparation of the nucleic acid sequence according to claim 10, **characterized in that** so many silent mutations are introduced into a nucleic acid sequence coding for a viral protein that the nucleic acid sequence thereby obtained contains monovalent restriction sites which make possible the exchange of the V2 and V3 regions.

39. (Withdrawn) Process for the preparation of the nucleic acid sequence according to claim 10, **characterized in that** so many silent mutations are introduced into a nucleic acid sequence coding for a viral protein that the nucleic acid sequence thereby obtained contains ten monovalent restriction sites at intervals of approx. 150 base pairs .

40. (Withdrawn) Process according to claim 38 , characterized in that the nucleic acid sequence coding for a viral protein is the sequence according SEQ ID NO: 1 or SEQ ID NO: 11 or a fragment of same.

41. (Withdrawn) Process for the preparation of the vector mixture according to claim 33, characterized in that plasmids, the nucleic acid sequences of which in each case differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop in each case through random distribution of the bases at the varied nucleotide positions, are ligated into a vector which can be expressed in host cells.

42. (Withdrawn) Process according to claim 41, characterized in that the host cells are *E. coli*, Cos, CHO or BHK cells.

43. (Withdrawn) Process for the preparation of the host cells composing transforming *E.coli*. with a vector mixture according to claim 30 .

44. (Withdrawn) Process for the preparation of a protein vaccine which comprises a mixture of viral protein molecules, characterized in that the molecules are sequence variants of a single viral protein or of part of same, the mixture containing $\geq 10^2$ sequence variants, which is obtainable by expression of a plasmid-DNA mixture which, because of the variation of nucleotide positions, contains randomly distributed sequence combinations, said process comprising cultivating host cells according to claim 35 under conditions which allow the expression of the mixture of viral protein sequence variants.

45. (Withdrawn) Process for the preparation of a DNA vaccine which codes for a mixture of structurally different virus proteins, characterized in that the vaccine contains a mixture of sequence variants of a viral DNA molecule or of part of same, the mixture containing $\geq 10^2$ DNA molecules which differ from each other in their nucleic acid sequence, where the mixture, because of the variation of nucleotide positions, contains randomly distributed sequence combinations wherein said process is carried out according to claim 41, wherein the plasmids are ligated into a vector which can be expressed in host cells of the organism to be vaccinated.

46. (Withdrawn) A method of preparing a vaccine comprising forming a mixture of structurally different viral proteins which are sequence variants of a viral protein or of part of same, for the prevention and/or therapy of a virus infection in humans.

47. (Withdrawn) A method of preparing a vaccine comprising forming a mixture according to claim 23 for the prevention and/or therapy of a HIV infection in humans.

48. (Withdrawn) A method of preparing a vaccine comprising forming a mixture of DNA molecules which code for sequence variants of a viral protein or of part of same, for the prevention and/or therapy of a virus infection in humans.

49. (Previously Presented) A method of preparing a vaccine comprising forming a nucleic acid mixture according to claim 19 for the prevention and/or therapy of a virus infection in humans.

50. (Previously Presented) A method of preparing a vaccine comprising forming the nucleic acid mixture according to claim 19 for the expression in host cells selected from the group consisting of *E. coli*, Cos, CHO and BHK cells.

51. (Previously Presented) A method of producing a protein mixture which comprises sequence variants of the GP120 protein, characterized in that it is a mixture of proteins which contain amino acid sequences which in each case differ from each other in the V2 loop and/or in the V3 loop, the mixture being obtainable by expression of a plasmid DNA mixture which, because of the variation of nucleotide positions, contains randomly distributed sequence combinations; said method comprising expressing a vector mixture which contains a mixture of plasmids which contains an inserted double-stranded DNA which comprises hybrids of the single-stranded nucleic acid sequence

according to claim 15 with a single-stranded nucleic acid sequence which contains the region coding for the V2 loop and/or the region of GP120 coding for the V3 loop, characterized in that in the V3 loop a 247 bp-long Bg1II-XbaI fragment or a 283 bp-long Bg1II-NheI fragment is exchanged for a modified fragment, and in the V2 loop a 139 bp-long PstI-Bc1I fragment or a 339 bp-long PstI-EcoRI fragment is exchanged for a modified fragment, the fragment/the fragments in each case containing inosine, a nucleic acid exchange or a mutation at at least 6 positions, the nucleic acid sequence being complementary to a nucleic acid sequence characterized in that it contains the sequence given in SEQ ID NO: 12; characterized in that the nucleic acid sequences of the plasmids differ in each case from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop, where the mixture of the plasmids, because of the variation of nucleotide positions, contains randomly distributed sequence combinations .

52. (Previously Presented) A method of preparing a protein mixture which comprises sequence variants of the GP120 protein, characterized in that it is a mixture of proteins which contain amino acid sequences which in each case differ from each other in the V2 loop and/or in the V3 loop, the mixture being obtainable by expression of a plasmid DNA mixture which, because of the variation of nucleotide positions, contains randomly distributed sequence combinations, said method comprising culturing a host cell according to claim 35 .

53. (Withdrawn) Pharmaceutical composition for the prevention and/or therapy of a virus infection, **characterized in that** it comprises a protein mixture and a nucleic acid mixture, the protein mixture comprising sequence variants of a viral protein or of part of same, and the nucleic acid mixture comprising DNA molecules which code for sequence variants of a viral protein or of part of same.

54. (Withdrawn) Pharmaceutical composition for the prevention and/or therapy of a virus infection, characterized in that it comprises a protein mixture and a nucleic acid mixture, the protein mixture comprising sequence variants of a viral protein or of part of same, and the nucleic acid mixture comprising DNA molecules which code for sequence variants of a viral protein or of part of same, said composition comprising a protein mixture according to claim 23 and a nucleic acid mixture which comprises double-stranded DNAs, the nucleic acid sequences of which are derived from the *env* sequence in SEQ ID NO: 1 or SEQ ID NO: 11 or a fragment of same, characterized in that the nucleic acid sequences in each case differ from each other in the region coding for the V2 loop and/or in the region coding for the V3 loop .